

**REMARKS**

Claims 1-4, 7 and 8 are pending in this application. Claims 5, 6, 9 and 10 have been canceled without prejudice or disclaimer. Claims 1 and 2 have been amended herein.

Claim 1 has been amended for clarity to recite “A food ... containing a mixture of ~~a plurality of peptides~~ an oligopeptide(s) having angiotensin converting enzyme inhibitory activity and a polypeptide”.

The mixture of amended claim 1 contains a hydrolyzate obtained by hydrolyzing fish meat with thermolysin enzyme and even when the substrate specificity of the enzyme is considered, it is evident that this hydrolyzate is “oligopeptide” and “polypeptide” derived from protein in the fish meat.

Moreover, claim 1 has been amended to recite that the treatment involves reducing “the content of polypeptide having a molecular weight of at least 5000 to at most 10 % by weight of the total ~~polypeptide~~ hydrolyzate in the mixture”. This clarifies that the basis for the “the content of polypeptide having a molecular weight of at least 5000” is the **hydrolyzate**. Support for this recitation may be found in the specification (substitute), for example, on page 3, second paragraph, and page 6, lines 13-17. A method for calculating the content of polypeptide having a molecular weight of at least 5000 by gel filtration chromatography is described in page 7, line 2, to page 8, second paragraph, of the present specification. From this method, it is evident that the content indicates the proportion based on hydrolyzate comprising oligopeptide and polypeptide.

In the hydrolyzate, not only “polypeptide” but also “oligopeptide” having fewer amino acids is included. “The content of polypeptide having a molecular weight of at least 5000” differs when the content is the proportion based on the “total polypeptide” and when the content is the proportion based on the “total hydrolyzate” which includes not only polypeptides but also oligopeptides.

This hydrolyzate is obtained by hydrolyzing dried bonito with thermolysin enzyme and even when the substrate specificity of the enzyme is considered, it is evident that this hydrolyzate is “oligopeptide” and “polypeptide” derived from protein in the fish meat.

As a result, the present invention is characterized in that angiotensin converting enzyme inhibitory activity and color equivalent to those of purified oligopeptide can be obtained, while the “bitterness” and “bad flavor” are lost. In contrast to purified oligopeptide, which has bitterness and bad flavor, the mixture of the present invention has no bitterness and good flavor. The reason for this lies in that the present invention includes not only oligopeptide but also polypeptide having at least a certain amount of amino acids. The differences between the present claims and the cited references are discussed in detail below.

**Claims 5 and 6 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite (Office action point 3).**

The rejection is moot in view of the cancellation of claims 5 and 6 without prejudice or disclaimer.

**Claims 1-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Masayasu (JP04069398) (Office action point 4).**

Reconsideration of the rejection of pending claims 1-4, 7 and 8 is respectfully requested in view of the amendments to the claims.

Masayasu '398 discloses obtaining a hydrolyzate (mixture) containing an oligopeptide having angiotensin converting enzyme inhibitory activity by hydrolyzing dried bonito with thermolysin enzyme. However, this hydrolyzate is later subjected only to condensation by centrifugation and not to any membrane treatment. Therefore, at this point, the content of polypeptide having a molecular weight of at least 5000 is **more** than 10% by weight of the total hydrolyzate in the mixture and clearly differs from the mixture described in the amended claim 1.

Also, the hydrolyzate of the reference is purified to obtain IVGRPRHQG (SEQ. ID No. 14) in claim 2 of the present application). However, the composition of the reference **does not include** "polypeptide" and therefore differs from the mixture of amended claim 1.

**Claims 1-10 remain rejected under 35 U.S.C. 102(b) as being anticipated by Yokoyama et al. (Office action point 5).**

Reconsideration of the rejection of pending claims 1-4, 7 and 8 is respectfully requested in view of the amendments to the claims.

Yokoyama et al. discloses obtaining a hydrolyzate (mixture) containing an oligopeptide having angiotensin converting enzyme inhibitory activity by hydrolyzing dried bonito with thermolysin enzyme. However, this hydrolyzate is later recovered by centrifugation as supernatant

A and is not subjected to any membrane treatment. Therefore, at this point, the content of polypeptide having a molecular weight of at least 5000 is **more** than 10% by weight of the total hydrolyzate in the supernatant A and clearly differs from the mixture described in the amended claim 1.

The hydrolyzate of the reference is purified to obtain an oligopeptide recited in claim 2 of the present application. However, the composition of the reference differs from the mixture of amended claim 1, as **“polypeptide” is not included** in the reference.

**Claims 1-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Suetsuna JP ‘692 (Office action point 6).**

Reconsideration of the rejection of pending claims 1-4, 7 and 8 is respectfully requested in view of the amendments to the claims.

Suetsuna ‘692 discloses obtaining LKWPIE having angiotensin converting enzyme inhibitory activity from a hydrolyzate (mixture) obtained by hydrolyzing sardines with pepsin enzyme. However, this oligopeptide does not correspond to any of the oligopeptides described in claim 2 of the present application.

Also, this hydrolyzate which contains oligopeptide having the inhibitory activity and polypeptide is treated by ultrafiltration, in which the exclusion limit is a molecular weight of 10,000. When fish meat is hydrolyzed by pepsin enzyme, the hydrolyzate is known to be bitter (cf. Yokoyama et al., page 1542, left column, 3<sup>rd</sup> line from bottom to 2<sup>nd</sup> line from bottom). Therefore,

the hydrolyzate (mixture) obtained by hydrolyzing with thermolysin enzyme of the present invention contains different oligopeptides and also clearly has different properties from that of Suetsuna.

Also, Suetsuna's hydrolyzate is purified by a column to obtain LKWPIE, but differs from the mixture of amended claim 1 as the obtained oligopeptide is different and **“polypeptide” is not included.**

#### **Further comments**

Applicants have above argued against anticipation of the pending claims by the cited references. Applicants further argue that the present invention has superior properties over the cited references that are not suggested by the references.

a) The purified oligopeptides described in Masayasu, Yokoyama et al. and Suetauna all have strong inhibitory activity and favorable color, but as described above, are known to have bitterness and bad flavor to those skilled in the art.

In contrast, the present invention aims to provide food containing an angiotensin converting enzyme inhibitor having inhibitory activity and color equivalent to those of purified oligopeptide without “bitterness” or “bad flavor”. The different and extremely superior effect of having inhibitory activity and color equivalent to those of purified oligopeptide without bitterness or bad flavor can be obtained by including “oligopeptide having inhibitory activity” and “polypeptide” in the mixture and “reducing the content of polypeptide having a molecular weight of at least 5000 to at most 10% by weight of the total hydrolyzate” (cf. Page 6, line 23, to page 7, line 1; Example 1, Table 1, and page 17, first paragraph of the substitute specification).

b) In Yokoyama et al., the supernatant obtained by centrifuging the hydrolyzate prepared by hydrolyzing dried bonito with thermolysin enzyme is described as “not having bitter taste or fishy odor”. This supernatant is obtained in practically the same manner as E-1 described in example 1 of the present specification. However, when E-1 is relatively compared with E-3, in which the content of polypeptide having a molecular weight of at least 5000 is reduced to at most 10% by weight of the hydrolyzate by membrane filtration, because the content of polypeptide having a molecular weight of at least 5000 in the hydrolyzate by membrane filtration, because the content of polypeptide having a molecular weight of at least 5000 in the hydrolyzate is defined, E3 showed strong inhibitory activity and good color and also significant improvement in bitterness and flavor. Furthermore, Yokoyama et al. has reached the conclusion that the supernatant does “not have bitter taste or fishy odor”, but does not disclose or even suggest that inhibitory activity and color equivalent to those of purified oligopeptide can be obtained and bitterness and flavor can be significantly improved by defining the content of polypeptide having a molecular weight of at least 5000 in the supernatant.

Also, several purified oligopeptides described in claim 2 of the present application are described in Yokoyama et al., but differ from the present invention in that these are mixtures of oligopeptide only and have bitterness and bad flavor.

Applicants therefore also submit that pending claims 1-4, 7 and 8 are non-obvious over the cited references.

Amendment under 37 CFR 1.111  
Hiroyuki FUJITA

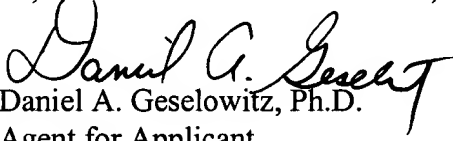
U.S. Patent Application Serial No. 09/663,709  
Attorney Docket No. 001200

Applicants submit that claims 1-4, 7 and 8, as amended, are in condition for allowance. If, for any reason, it is felt that this application is not now in condition for allowance, the Examiner is requested to contact Applicant's undersigned agent at the telephone number indicated below to arrange for an interview to expedite the disposition of this case.

In the event that this paper is not timely filed, Applicant respectfully petitions for an appropriate extension of time. Please charge any fees for such an extension of time and any other fees which may be due with respect to this paper, to Deposit Account No. 01-2340.

Respectfully submitted,

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